UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,362	03/12/2004	William M. Pardridge	407J-002000US	9026

22798 7590 12/14/2006

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
WOLLENBERGER, LOUIS V	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/800,362	PARDRIDGE ET AL.	
	Examiner	Art Unit	
	Louis V. Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006 and 08 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Location of the Application

The location of the application has changed. The application has been docketed to Examiner Louis V. Wollenberger in Art Unit 1635.

Election/Restrictions

Applicants' remarks regarding the Restriction Requirement of 11/10/05 are noted; however, as noted in the previous Action, Applicants' election was treated as an election without traverse since no remarks pointing out the supposed errors in the restriction were presented in Applicants' response filed 12/9/05.

To be clear, the shRNAs recited in claim 2 are considered to represent independent and distinct inventions, not species, because they correspond to structurally and functionally distinct compounds, i.e., polynucleotides, with different designs and effects inasmuch as they would result in the inhibition of different genes and would produce different biological effects in the cell and organism. The different shRNAs lack unity of invention under the rules and guidelines of Restriction Practice in that they do not share a substantial structural feature essential to their utility—they target different genes and would be expected to comprise different nucleotide sequences. Further, according to MPEP §803.04, polynucleotide molecules defined by their nucleic acid sequence that encode different proteins are structurally distinct chemical compounds. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 USC §121.

Nevertheless, the Examiner acknowledges Applicants' remarks regarding the restriction as applied to the targets of claim 2, and notes that Claim 1 links the inventions of claim 2.

Accordingly, the restriction requirement among the linked inventions is **subject to** the nonallowance of the linking claim(s), claim 1. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Status of Application/Amendment/Claims

Applicant's response filed 6/8/06 to the Non-Final Action of 3/8/06 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 3/8/06 are hereby withdrawn. The following rejections and/or objections are either newly applied or are

reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 9/14/06, claims 1-17 are pending and under examination.

Claim Objections—withdrawn

The objections to Claims 4, 5, 17 are withdrawn in view of Applicants' amendments to the claims.

Claim Rejections - 35 USC § 112, second paragraph—withdrawn

The rejection of Claims 3-6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of Applicants' amendments to the claims.

Claim Rejections - 35 USC § 112, first paragraph—withdrawn

The rejection of Claims 1-17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicants' amendments to the claims.

Claim Rejections - 35 USC § 102—withdrawn

The rejection of Claims 1, 7, 16 and 17 under 35 U.S.C. 102(b) as being anticipated by Talke et al. (US 5,891,689) is withdrawn in view of Applicants' amendments to the claims.

***

The rejection of Claims 1 and 7-17 under 35 U.S.C. 102(a) as being anticipated by Zhang et al. (2003) *J Gene Med.* 5:1039-1045 is withdrawn in view of the declaration under 37 CFR 1.132, filed 6/8/06, indicating that applicants are the sole inventors and that the others named in the Zhang et al. reference were merely working under their direction. Thus, the under 37 CFR 1.132 filed 6/8/06 is sufficient to overcome the rejection of claims 1 and 7-17 based upon Zhang et al. (2003).

***

The rejection of Claims 1–13 and 15-17 under 35 U.S.C. 102(e) as being anticipated by McSwiggen et al. (US 2004/0192626 A1), as evidenced by Zhang et al. (2002) *J. Gene Med.* 4:183–194 is withdrawn in view of Applicants' amendments to the claims and in view of Applicants' arguments, which are found persuasive in part.

Claim Rejections - 35 USC § 103—maintained

Claims 1, 2, and 7–17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (2002) *J. Gene Med.* 4:183-194, Shi et al. (2001) *PNAS* 98:12754–12759, and Paddison et al. (2002) *PNAS* 99:1443–1448.

Response to Arguments

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In the instant case, the cited references are relied upon as a whole for what they teach or reasonably suggest to one of skill in the art at the time the invention was made.

Applicants challenge the references individually, pointing out deficiences in each with regard to the invention as a whole.

Applicants argue that Zhang et al. (2002) relates to a completely different technology, that antisense RNA is not an shRNA, that one would have had no way of knowing whether results similar to Zhang et al. (2002) could be achieved using an shRNA, and that there is simply no way of equating anti-sense and shRNA technologies. Applicants state that there was not a single previous demonstration of an increase in survival from cancer of any type with intravenous shRNAi gene therapy (Remarks, pp. 11-12).

These arguments are not persuasive because Zhang et al. expressly teach that EGF receptor mRNA is overexpressed in many cancers, including high-grade brain gliomas, and that antisense RNA directed to EGFR mRNA can reduce cell proliferation and growth of EGFR-dependent gliomas. Accordingly, one of skill in the art would recognize that, with regard to the treatment of cancer, EGFR is an effective target and the inhibiting the expression of EGFR is an effective method for reducing tumor cell growth. With the disclosure of Paddison et al., one of

many in the RNAi art, one of skill would recognize that dsRNAs, in the form of either siRNA or shRNA, are, in general more effective than antisense RNAs as inducers of gene silencing. This is expressly stated on page 948 of Paddison et al. Moreover, the Paddison et al. report documents the potency and effectiveness of inducing RNAi-mediated gene silencing using plasmid-encoded shRNA, known and recognized to be a mediator of RNAi in mammalian and vertebrate cells. There is absolutely no ambiguity in this report with regard to the overall potency and versatility of shRNA for inhibiting the expression of virtually any known gene. Inasmuch as both Zhang et al. and Paddison et al. both show that both shRNAs and antisense RNAs can be expressed from plasmids transfected into cells, one of skill in the art would immediately recognize that the antisense plasmids of Zhang et al. could be replaced by nearly any other plasmid or gene therapy vehicle, including the shRNA-encoding plasmids of Paddison et al. One of skill in the art would have been motivated to make and use shRNA-encoding plasmids according to Paddison et al. for targeting EGFR as taught by Zhang et al. given that Zhang et al. show that the inhibition of EGFR expression is an effective anti-cancer treatment.

The Examiner agrees that antisense and RNAi technologies have mechanistic differences and involve nucleic acids with different structures; however, both technologies have an art-recognized suitability for an intended purpose of inhibiting gene expression. Additionally, there is an art-recognized equivalency inasmuch as both technologies make use of relatively short oligonucleotides with similar chemical makeups and having similar requirements with regard to target recognition and binding. Nevertheless, the art recognizes the advantages of increased potency and, possibly, stability, of dsRNAs, as evidenced by Paddison et al., and that siRNAs

and shRNAs as forms of dsRNAs are effective for inducing gene expression inhibition in mammalian cells.

Applicants' arguments that the combination of Shi (2001) and Paddison (2002) with Zhang (2002) do nothing to provide elements of the invention absent from Zhang (2002), that Shi et al. (2001) does not describe compositions for the inhibition of gene expression, and that Paddison (2002) relates to compositions for in vitro delivery of shRNA that are entirely unrelated to the compositions of the present invention (Remarks, page 12), are not persuasive since, again, when viewed as a whole, the combination of references teaches and/or reasonably suggests the claimed invention as whole with all its limitations, including the use of pegylated immunoliposomes comprising monoclonal antibodies targeted to humun insulin receptor for delivering shRNA-encoding, EGFR targeted plasmids or expression constructs to brain gliomas for inhibiting the expression of EGFR in brain gliomas, as well as related brain cancers.

Zhang et al. exemplifies "receptor-specific nanocontainers" as now claimed for use with antisense-encoding vectors and states that their pegylated immunoliposome technology "allows for widespread gene expression in the brain *in vivo* following the intravenous injection of non-viral gene formulations..." (page 193, left, bottom). They state further that " The expression of thereapeutic genes may be restricted to brain cancer *in vivo* following intravenous administration of the exogenous gene with the combined use of tumor-specific gene promoters and gene targeting technology using PILs" (page 193, right, top).

Accordingly, one of skill in the art would have been motivated and have had a reasonable expectation of success in adapting the Zhang et al. technology and cancer treatment strategy for the delivery of RNAi constructs such as those exemplified by Paddison et al.. The disclosure of

Shi et al. bolsters the disclosure of Zhang et al., describing brain-specific delivery of a "therapeutic gene" using PILs conjugated to the transferrin receptor, providing additional evidence of the intrinsic properties and versatility of PILs for delivering plasmid DNA to specific cellular and organ targets.

Finally, Applicants argue that the rejection fails to establish a motivation to combine the references, and that nothing in the art itself suggests the particular combination of references made by the rejection, resulting in impermissible hindsight reconstruction (Remarks, page 13).

Applicant's arguments have been fully considered but they are not persuasive.

The Examiner notes there are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art (MPEP 2143.01, Section I).

The Examiner notes that the test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art (MPEP 2143.01, Section I).

The Examiner notes that any judgement on obviousness is in a sense necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper.

Finally, the Examiner notes there is no requirement that an express, written motivation to combine must appear in prior art references before a finding of obviousness. For example,

motivation to combine prior art references may exist in the nature of the problem to be solved or the knowledge of one of ordinary skill in the art (MPEP 2145, Section X, Part A).

In the instant case, one of skill in the art of gene therapy and cancer biology, for example, at the time the invention was made would have been commended to the relevant teachings in the prior art describing and exemplifying the use of antisense and RNAi technology to inhibit gene expression and thereby treat aberrant gene expression as it concerns human disease such as cancer. One of skill would understand upon a review of the instant references that both antisense and RNAi are alternative strategies for mediating gene expression inhibition, but that RNAi has certain inherent advantages—primarily, potency. Further, one of skill would have recognized that Zhang et al. together with Shi et al. provide an effective delivery system for administering mRNA expression inhibiting oligonucleotides to the brain tissues of patients affected by brain cancer and that EGFR is one possible target with utility for treating brain cancer.

Therefore, the motivation to combine is implicit: it exists in the nature of the problem to be solved—tissue and cell specific delivery and uptake of therapeutic nucleic acids for the treatment of cancer—as well as the knowledge of one skill in the art, who would know that the PIL systems and RNAi constructs described in the aforementioned prior art references could be readily manipulated, modified, and combined to produce a working RNAi-competent embodiment targeted to EGFR, an embodiment within the scope of the instantly claimed invention.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 103—new

Claims 3–6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (2002) *J. Gene Med.* 4:183-194, Shi et al. (2001) *PNAS* 98:12754–12759, and Paddison et al. (2002) *PNAS* 99:1443–1448 as applied to claims 1, 2, and 7–17 above, and further in view of Bennet et al. (U.S. Patent 5,914,269), Tuschl et al. (US 2004/0259247), Bass (2001) *Nature* 411:428-9; and Vickers et al. (2003) *J. Biol. Chem.* 278: 7108–7118.

Claims 3–6 limit the invention by stating that short hairpin RNA comprises a nucleotide sequence antisense to a portion of human EGFR mRNA comprising SEQ ID NO:21.

Applicants' Remarks, page 8, top, states that SEQ ID NO:21 corresponds to GenBank Acc. No. X00588.

Zhang et al. (2002) *J. Gene Med.* 4:183-194, Shi et al. (2001) *PNAS* 98:12754–12759, and Paddison et al. (2002) *PNAS* 99:1443–1448 are relied on for the reasons given above.

Bennet et al. teach antisense oligonucleotides for inhibiting the expression of human EGFR corresponding to GenBank Accession No. X00588 (col. 14, Example 7). Bennet et al. teach that a number of malignant and non-malignant disease conditions are now believed to be associated with EGFR, particularly aberrant expression of EGFR (col. 1). Bennet et al. teach a variety of methods and materials for making and using antisense oligonucleotides targeted to EGFR and teach that oligonucleotides targeted to EGFR can effectively reduce EGFR expression and thereby inhibit malignant cell growth in culture and in animals in some circumstances. Bennet et al. devote considerable disclosure to methods of administering EGFR oligos for cancer

therapy purposes. For example, Bennet et al. teach that oligodeoxyribonucleotides complementary to mRNA targeted to EGFR have been encapsulated into liposomes linked to folate via a polyethylene glycol linker and delivered into cultured human epidermoid carcinoma KB cells and that these oligonucleotides reduce cell proliferation (col. 1).

Tuschl et al. teach the materials and methods for making and using short double-stranded RNA molecules for inhibiting the expression of virtually any known gene via RNA interference (RNAi) in mammalian cells, including human cells (paragraphs 10, for example). It is taught that double-stranded RNA molecules 19-25 nucleotides in length have RNAi activity and may trigger the specific degradation of homologous RNAs within the region of identity with the dsRNA (paragraphs 5, 7, 11, and 17 for example). Tuschl et al. teach that siRNA duplexes are preferably composed of 21-nt antisense siRNAs and should be selected to form a 19-bp double helix with 2-nt 3' overhanging ends (paragraphs 9, 11, 179).

Tuschl et al. teach that dsRNA molecules may be chemically or enzymatically synthesized using methods known in the art (paragraphs 20-24, 97, 141), or expressed from vectors (paragraph 39).

Tuschl et al. teach that dsRNAs may be formulated in pharmaceutically acceptable compositions for use in therapeutic applications (paragraph 31-33).

In summary, the Tuschl et al. reference is considered to be a complete blueprint for the design, synthesis, and use of short interfering, double-stranded RNA, in modified or unmodified forms, against any desired target gene. The reference contains detailed descriptions and several examples typifying the use of siRNA in cell culture, and the Application Publication expressly suggests the use of siRNA *in vivo* for use in therapeutic and clinical settings (paragraphs 31-36).

Importantly, Tuschl et al. also compare siRNA methodology to that of antisense and ribozyme techniques for inhibiting gene expression. At paragraph 148, for example, Tuschl et al. state that siRNAs are extraordinarily powerful reagents for mediating gene silencing and that siRNAs are effective at concentrations that are several orders of magnitude below the concentrations applied in conventional antisense or ribozyme gene targeting experiments. At paragraph 137, Tusch et al. state that the remarkable finding that synthetic 21 and 22 nt siRNA duplexes can be used for efficient mRNA degradation provides new tools for sequence-specific regulation of gene expression in functional genomics as well as biomedical studies. The siRNAs may be effective in mammalian systems where long dsRNAs cannot be used due to the activation of the PKR response. As such, the siRNA duplexes represent a new alternative to antisense or ribozyme therapeutics.

Bass teaches that, like some antisense oligonucleotides, which trigger RNase H-catalyzed cleavage of their targets, siRNAs trigger the degradation of complementary messenger RNAs (page 428 and Fig. 1). A general outline of the RNAi mechanism is taught, showing how siRNA-mediated RNAi may be used to interfere with gene expression using siRNAs directed against specific mRNA sequences (Fig. 1). Bass teaches that RNAi has repeatedly proven itself to be more robust that antisense techniques: it works more often, and typically decreases expression of a gene to lower levels, or eliminates it entirely. Furthermore, siRNAs are effective at concentrations that are several orders of magnitude below the concentrations typically used in antisense experiments.

The prior art teaches, in general, then, that siRNAs and antisense oligonucleotides can be used to produce the same effect, albeit with different potencies and by different biochemical

mechanisms. siRNAs and antisense oligos can both be used to inhibit gene expression *in vivo* or *in vitro*, via mRNA degradation or translation attenuation, and, thus, both types of nucleic acids may be used to prevent the expression of a gene in a cell. For example, Bass teaches that antisense RNA is another technique to prevent the expression of particular genes (page 429). Thus, in this sense, siRNAs and antisense oligos are art-recognized equivalents that may be used for the same purpose: reducing or inhibiting gene expression. (See for example MPEP §2144.06, SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE.)

Nevertheless, as explained above, siRNAs possess certain advantages over antisense oligos, which would motivate one of ordinary skill in the art to select siRNAs over antisense oligos to more efficiently block and/or reduce the expression of any given target gene, particularly a gene known to be involved in cancer.

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to use siRNAs, as taught by Tuschl et al. and Bass, for inhibition of EGFR expression, including EGFR mRNA corresponding to GenBank Acc. No. X00588, SEQ ID NO:21, as taught by Zhang et al. and as more specifically suggested and exemplified by Bennet al. for the reasons given by Zhang et al., cited above and Bennet et al.

With regard to claims 4–6, which require that the shRNA comprise a sequence that is antisense to a portion of EGFR mRNA located between nucleotides 2300 and 3800, 2500 and 3000, and 2500 and 2600 of SEQ ID NO:21, Zhang et al. teach an antisense RNA targeted to a region corresponding to nucleotides 2317–3006 of human EGFR cDNA derived from the pE7 plasmid (page 185), and Bennet et al. teach antisense oligonucleotides targeted to nucleotides 2966-2985 of human EGFR (SEQ ID NO:21) (Table 1, cols. 13-14).

Vickers et al. compare and contrast the properties and functions of antisense oligonucleotides and siRNAs targeted to the same gene. Vickers et al. teach in general that sites on a target RNA that are not active with RNase H-dependent oligonucleotides are similarly not good sites for siRNA. Conversely, a significant degree of correlation between active RNase H oligonucleotides and siRNA was found, suggesting that if a site is available for hybridization to an RNase H oligonucleotide, then it is also available for hybridization and cleavage by the siRNA complex (page 7116, for example, but see throughout).

Accordingly, in view of Vickers et al., one of skill in the art would be motivated to design and use shRNAs based on the sequences targeted by the antisense RNAs and oligonucleotides disclosed by Zhang et al. and Bennet et al.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LVW
December 8, 2006

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER